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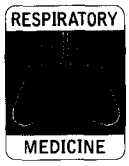

Topical Review

Nutritional support in advanced pulmonary disease

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Advanced pulmonary disease (APD), often secondary to emphysema or chronic bronchitis, is generally a progressive, incurable condition, ultimately leading to death. The condition is associated with significant, distressing symptoms. Most APD patients are underweight, which has numerous implications including accentuation of reduced physical capacity during daily life, increased risk of other secondary diseases, e.g. infections and osteoporosis, and a higher mortality during exacerbations with acute respiratory failure. Consequently, careful nutritional support is crucial both in enhancing physical well-being and function, and in reducing the risk of acute respiratory failure. Knowledge concerning the exact nutritional needs in APD is still very sparse; however, specific actions against malnutrition in APD patients should be mandatory in the treatment of APD. This paper reviews the literature concerning implications of malnutrition and benefits of nutritional support in APD patients, and gives suggestions for the practical, daily-life nutritional management of APD.

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Introduction

Advanced pulmonary disease (APD), usually secondary to emphysema or chronic bronchitis, is generally a progressive, incurable condition, ultimately leading to death. The condition is associated with significant, distressing symptoms, several of which are worsened by malnutrition. In COPD patients, between 30 and 70% have clinical evidence of undernutrition (1–3), whereas the frequency of overweight patients with APD is much lower. Adverse effects of undernutrition include weakened respiratory muscles, decreased ventilatory drive and altered lung defences. Overnutrition, on the other hand, is associated with increased carbon dioxide production, which increases the amount of ventilation necessary to maintain steady-state arterial blood gases (4).

Nutritional management is crucial in the management of APD in preventing or treating possible deleterious effects, such as worsening of the reduced physical capacity during daily life, increase of the risk of other secondary diseases, e.g. infections and osteoporosis, and contribution to a higher mortality during exacerbations resulting in acute respiratory failure. The only data specifically concerning nutritional management in APD patients were dealing with situations with acute respiratory failure (5,6). Few papers have dealt specifically with the daily-life nutritional management of APD patients, and only desultory data are available. In this review, suggestions for a rational nutritional management of APD are presented.

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Implications of Malnourishment in APD

In chronic obstructive pulmonary disease (COPD) patients, reduced respiratory strength has been proved (7) along with generalized muscle weakness. Approximately 50% of the energy used by the diaphragm is derived from carbohydrate oxidation (8). As the glycogen stores are depleted in undernutrition, the body in the catabolic state utilizes the skeletal muscles,

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including the diaphragm and intercostals, as fuel. A reduced diaphragmatic mass is a consequence both in health and disease (9,10), and malnourished patients without pulmonary disease have decreased respiratory muscle strength (7,11). In emphysematous patients, low body weight was correlated with low diaphragmatic mass (9), and in a necropsy study, it was demonstrated (10) that in poor nourishment, body weight and diaphragm muscle mass was reduced to 70 and 60% of normal, respectively. Body weight in COPD patients has been found to be a powerful predictor of diffusing capacity, and seems to influence mortality, independent of forced expiratory volume in 1 s (FEV_1) (12). A possible influence on the ventilatory drive is suggested from a study in normal subjects with semi-starvation (13), in whom a 42% reduction of the ventilatory response to hypoxia was found. Re-feeding returned the hypoxic drive to baseline. Similar observations in APD patients are not available. Other positive effects of re-feeding in COPD patients have been demonstrated. In a randomized study, enteral re-feeding, equal to 1000 kcal day^{-1} above usual intakes, was associated with both weight gain and improved respiratory muscle strength (14). In a 9-month prospective study, malnourished patients were given a surplus of oral food attaining 25% extra energy and 50% extra protein during the middle 3 months of the study (15). As compared with a similar group of patients having the usual diet for all 9 months, the intensive-treated group gained clinical improvement such as general well-being, breathlessness scores, and improved 6-min walking distance (15).

Malnourishment in APD may also increase the risk of infections. Suppressed cell-mediated immunity is the most profound effect (16). In rats, the *in vivo* pulmonary defence against organisms cleared by T-lymphocytes, e.g. Listeria monocytogenes, was markedly impaired (17). The macrophage function was reduced after starvation (18), and recovery of function as a response to re-feeding was delayed for up to 3 weeks. In patients with long-term tracheostomies (19), poor nutritional status was noted to have a greater degree of bacterial binding to lower airway cells. The data indicate that malnourishment can alter cellular resistance of tracheobroncial mucosa to bacterial infection.

Along with age, smoking history and use of steroids, osteoporosis is exceedingly common in APD. The condition will be accelerated in malnourishment due to low vitamin D and calcium intake, and due to the general catabolic condition. Osteoporosis has possible influences because of pain due to fractures, resulting in decreased respiratory depth, increasing the risk of infections (1).

Estimation of the Nutritional State

WEIGHT AND LEAN BODY MASS

As mentioned above, the vast majority of APD patients are malnourished. The estimation of body weight as ideal *vs.* underweight, however, is not without problems. The methods used should be cheap, easy to perform, without discomfort for the patients and serial measurements of the parameters should give information concerning changes in body mass and composition. Most studies have compared the actual body weights with standardized tables, typically from insurance companies, e.g. the Metropolitan Life Insurance Tables based on the 1979 Build Study (20). These tables report relative body weights that do not necessarily reflect over- or underweight. The studies on which these tables are based were flawed in many ways, including the skewed population studied, the unit of analysis, i.e. the length of time of follow-up, the failure to consider important variables such as smoking, the failure to measure frame size, and the fact that approximately 10% of the data were self-reported. None of the studies considered the distribution of body fat or muscle mass. A more specific measurement is the individual weight loss from the start of the disease and recent weight changes, the latter being a major sign of malnutrition. Recent loss of more than 10% of the habitual body weight reflects severe malnutrition (5), but factors such as dehydration and oedema should, however, be kept in mind when evaluating the changes in lean body weight (LBM). Body weight is the parameter that should be used in serial measurements during hospitalization, since other anthropometric measures, such as triceps skin-fold thickness, are

not sensitive to short-term (less than 2 weeks) changes (6).

Loss of skeletal muscle mass is a crucial factor in the malnourished APD patient. Estimation of the relative muscle mass and, especially, loss of muscle mass are useful tools. The serum albumin concentration can be used as an indicator of the muscle mass, but has several limitations, e.g. the production is depressed in acute illness. Since the circulating half-life of albumin is 18 days, nutritional changes will not be reflected until after several weeks. Other proteins with shorter half-lives, such as transferrin, have been suggested as indicators of protein balance (5). Bioelectrical impedance, which can be used as a bed-side measurement, gives an estimate of the actual LBM, and has a high correlation (0·9–0·97) with fat-free body mass by density measurements (21). The measure is only useful in static measurements and cannot be used in situations with rapid changes in body mass (21–23). A simpler method of estimating LBM is to measure the 24-h excretion of creatinine. Thus, on an *ad libitum* diet, it has been demonstrated that LBM in kg=0·021 Cr (mg day^{-1})+7·38, with an r value of 0·97 (24). To achieve a qualified expression of LBM from this equation, several points must be given attention. The subjects should eat a meat-free diet for 2 days prior to the urine collection (CV% of urinary creatinine is 2–19%), the collection time should be accurate, the collection should be complete, and the bladder should be completely empty. The 24-h creatinine excretion is altered in conditions of trauma and sepsis (25).

BIOCHEMICAL MARKERS

Apart from urinary creatinine, several simple laboratory measurements can be used to further evaluate a patient's nutritional status, including standard tests for kidney and liver function, and blood cell count. Of special interest are the levels of the divalent ions calcium, magnesium and phosphate, since the body stores are often depleted in severely malnourished patients. Depletion of these ions is associated with respiratory muscle weakness (26–29).

To monitor the adequacy of protein intake, the nitrogen balance can be estimated as: dietary nitrogen − excreted nitrogen − insensible nitrogen loss. Dietary nitrogen is calculated by dividing the intake of protein in grams by 6·25. Urine urea nitrogen represents 80–90% of total urinary nitrogen loss, and excreted nitrogen is then calculated as 1·2 times the urine urea nitrogen. The urine collection should be accurate and complete. In renal failure with creatinine clearance below 20 ml min^{-1}, determination of nitrogen balance by urinary urea collection is not accurate (30). The insensible nitrogen loss due to skin and stool loss is usually about 2 g day^{-1} but should be increased if the patient has diarrhoea, skin loss or wounds (6).

What are the Nutritional Requirements?

ENERGY

Two matters are interesting in this context; the daily intake of food and the actual needs. The daily intake can be measured by various techniques, but could preferably be performed by a dietitian to validate the reported intakes from the patient.

In nutritional studies, the most accurate (i.e. with the lowest coefficient of variation) method for assessing food consumption is the record with weights of foods (31). While 24-h recalls are not recommended, there is no statistical justification for extending the length of recording for longer than 3 days, randomized to cover each day of the week (31). A reliable measurement of the salt consumption urine analysis is a preferable method (31), and estimation from food recordings is not possible.

The actual needs of energy can be estimated by calculation or by means of indirect calorimetry. The latter gives an estimation of the energy expenditure during the test, by measuring the oxygen consumption and carbon dioxide production using a ventilated hood system. However, the method demands a high degree of standardization of the test conditions, periods of measurement of 6–24 h, and is only recommended in selected patients (5). Thus, this method should be viewed as an investigative tool and cannot be seen as the daily method of use. The resting energy expenditure (REE) is largely determined by the energy consumption of the brain, liver, kidneys and heart, for which reason it may be expected that the REE depends on the

body size. Several studies have in fact demonstrated that the REE is highly correlated with the fat-free body mass (LBM) (32). Calculation of the energy requirements can be estimated by the Harris-Benedict equation (33), which relates the REE (kcal) to the age, gender and body size:

REE (men): 66·5+13·75W+5·003H+6·775A
REE (women): 665·1+9·563W+1·850H+4·676A

where W is weight in kilograms, H is height in centimetres, and A is age in years.

The basal equation can be multiplied by 'stress factors' in seriously ill patients, or by 'activity factors' to compensate for the increased energy needs with physical activity. While most APD patients have a fairly sedentary life, an activity correction would not be necessary in most circumstances. In a study of ventilated COPD patients with acute respiratory failure (34), it was found that the stress factors ranged from 29 to 54%. Studies in COPD patients (35,36) have suggested that hypermetabolism can, at least in part, explain the weight loss seen in these conditions; however, the phenomenon is under discussion (37). In healthy subjects with semi-starvation, an adaptive process to weight loss was suggested (38), as decreased total oxygen consumption exceeded the decrease in body mass. In contrast, Schols *et al.* demonstrated in COPD patients that similar absolute values of REE, estimated by indirect calorimetry, were found between weight-losing and weigh-stable patients despite a decrease in LBM (36), indicating that no adaptive process is found in COPD patients during weight loss. Interestingly, malnourished emphysema patients achieved normal nutritional status 6 months to 1 yr after lung transplantation (39), which corroborates the theory concerning a defectiveness in adjusting the energy expenditure to changes in body weight. The ratio between the measured and calculated (by the Harris-Benedict equation) REE was around 1·17 and 1·08 ($P<0·005$) in the weight-losing and weight-stable patients, respectively (36). These data indicate that the calculated energy needs in COPD patients exhibiting weight loss ought to be calculated from the desired body weight rather than from the lowered, actual body weight, or should initially be set around 15% higher than predicted from the calculations.

PROTEIN

Protein needs are around 1–2 g kg^{-1} day^{-1} corresponding to approximately 20% of total energy, and in malnourished patients, a positive protein balance is the goal (5,6). The use of exogenous protein as a substrate for anabolism is energy dependent, and requires non-protein calories as carbohydrate or fat. Typically, 25–35 kcal of non-protein calories are necessary for the metabolic use of each gram of protein (5).

Glucose may spare protein breakdown more than fat. A potential disadvantage of such a high intake of carbohydrate is increased carbon dioxide production due to increased lipogenesis and respiratory quotient. The practical significance of increased carbon dioxide production in APD patients is, however, not entirely known. In COPD patients, neither a glucose load (40) nor a meal with high (80%) content of carbohydrate (41) had an influence on the arterial carbon dioxide pressure. On the other hand, Brown *et al.* (42) found that the timed walking distance was shorter after a large carbohydrate load in COPD patients. Fat requirements should be balanced in order to fulfil the needs of essential fatty acids, e.g. linoleic acid. Complications of high-fat administration include possible fatty infiltrates of the liver, as suggested by elevated values for liver function tests (43). Furthermore, development of abdominal obesity is a theoretical risk, resulting in decreased FEV_1, increased arterial carbon dioxide and decreased arterial oxygen (44).

The appropriate combination of fat and carbohydrate should be decided individually according to the actual patient characteristics. Thus, fewer carbohydrates may be appropriate in a poorly nourished patient with COPD than in a normally nourished patient with adult respiratory distress syndrome (6). No studies concerning the optimal composition of the diet in APD patients without acute respiratory failure are available. For ventilated patients with respiratory failure, a caloric profile of 20% protein, 50–60% carbohydrate and 20–30% fat have been suggested (45). These recommendations may be the composition that could be generally

recommended, since it is very close to what is recommended to the population in general by the American Heart Association (46).

As it has been demonstrated that a contributing factor to malnourishment in COPD patients is an inadequate dietary intake for energy expenditure (36), factor promoting a sufficient intake of food are important. This includes, of course, simple factors such as food items as desired individually, the food should be served in an appetising and tempting way, and the food should be palatable. Furthermore, the patient should not have any discomfort with breathing during meals. The possibility of oxygen desaturation during meals should be given attention. Thus, in COPD patients with normoxaemia, small desaturations in the first 20 min after meals were found (41). In hypoxaemic patients, however, oxygen saturations fell from a mean value of 87 to 80% during the initial 10 min postprandially (41), for which reason while increasing oxygen supply in some patient might be advantageous.

Conclusion

Malnourishment in APD patients is common and has several potentially serious implications. Most of the adverse effects of undernutrition seem to be, at least partially, reversible in response to re-feeding. By cheap and simple methods, the nutritional status can be evaluated, and the effects of re-feeding can be monitored. In the daily treatment of APD patients in stable conditions, specific actions towards a good nutritional status should be instituted. Large-scale studies of the effects of re-feeding in APD patients would be desirable.

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